CTCGGGAGCTGCTGGCAAAGAAGACCCACACCTCACAAATTGAAGTGATCCCTTGCAAGATCTGTGG GGACAAGTCATCTGGGATCCACTACGGGGTTATCACCTGTGAGGGGTGCAAGGGCTTCTTCCGCCGCAGC CAGCAGTGTAATGTGGCCTACTCCTGCACGCGTCAGCAGAACTGCCCCATTGACCGAACCAGCCGCAACC GATGCCAGCATTGCCGCCTGCAGAAGTGCCTGGCTCTGGGCATGTCCCGAGATGCTGTCAAGTTTGGCCG AATGTCCAAGAAGCAGAGGGACAGTCTACATGCAGAAGTGCAGAAACAACTGCAACAGCAGCAGCAACAG CAGATGGGCAGCTACCACTGGGCGCCTCACCTGACCTACCCGAGGCCTCTGCTTGTCCCCCCTGGCCTCCT GAGAGCCTCAGGCTCTGGCCCACCATATTCCAATACCTTGGCCAAAACAGAGGTCCAGGGGGCCTCCTGC CACCTTGAGTATAGTCCAGAACGAGGCAAAGCTGAAGGCAGAGACAGCATCTATAGCACTGACGGCCAAC TTACTCTTGGAAGATGTGGACTTCGTTTTGAGGAAACCAGGCATCCTGAACTTGGGGAACCAGAACAGGG GAGTACCTGGTACAGAATGTCTGCAAGTCCTTCCGAGAGACATGCCAGCTGCGACTGGAGGACCTTCTAC GGCAGCGCACCAACCTCTTTTCACGGGAGGAGGTGACCAGCTACCAGAGGAAGTCAATGTGGGAGATGTG GGAGCGCTGTGCCCACCACCTCACTGAGGCCATTCAGTATGTGGTGGAGTTTGCCAAGCGGCTTTCAGGC TTCATGGAGCTCTGCCAGAATGACCAGATCATACTACTGACAGCAGGAGCAATGGAAGTCGTCCTAGTCA GAATGTGCAGGGCCTACAATGCCAACAACCACACAGTCTTTTTTGAAGGCAAATACGGTGGTGTGGAGCT GTTTCGAGCCTTGGGCTGCAGCGAGCTCATCAGCTCCATATTTGACTTTTCCCACTTCCTCAGCGCCCTG TGTTTTTCTGAGGATGAGATTGCCCTCTACACGGCCCTGGTTCTCATCAATGCCAACCGTCCTGGGCTCC AAGAGAAGAGGAGAGTGGAACATCTGCAATACAATTTGGAACTGGCTTTCCATCATCATCTCTGCAAGAC TCATCGACAAGGCCTCCTAGCCAAGCTGCCACCCAAAGGAAAACTCCGGAGCCTGTGCAGCCAACATGTG GAAAAGCTGCAGATCTTCCAGCACCTCCACCCCATCGTGGTCCAAGCCGCCTTCCCNCCACTCTATAAGG TTTCCTTCAGCCCTCTGACCCGTCTCCCTGGACTCCCTTCACCCAGCCTTTCCCCTTTCTGCACTCTATGA AGGGTGGTATCCCTAGGAGTAAGCAAATCCTAAGACTGATTTTCTGCCCCTAGGCTTGCCTTGTAGGACA ACAGCAGCAAGTGATGGAGAAAAGGCTTGTTATGTTTGATTTCCCATAAGTTCCACCCTGGCTTCTGGAA GCTGTGGGGTAGATGGGATAGAGATAGGATGACCAAGTCAAATAAAAACAGACTGACAATCAGCAGGGA TAAATCCAGGTACCTGGGATAAGGAGAACTCAAATCTAGGCTTGAAAGCTAATAACAGTCCTTTCAATAC CTCATTGTATTTCCCCATGGGTCCTCCTGGGGGGACATGGATCTAGCTCAGAGACTGGTGGCAAGCCCCC AGAAGGACCTGTATATAATAAGAATATAGATTCCTG (SEQ ID NO:1)

MDRAPQRHHRTSRELLAAKKTHTSQIEVIPCKICGDKSSGIHYGVITCEGCKGFFRRSQQCN VAYSCTRQQNCPIDRTSRNRCQHCRLQKCLALGMSRDAVKFGRMSKKQRDSLHAEVQKQ LQQQQQEQVAKTPPAGSRGADTLTYTLGLSDGQLPLGASPDLPEASACPPGLLRASGSGPP YSNTLAKTEVQGASCHLEYSPERGKAEGRDSIYSTDGQLTLGRCGLRFEETRHPELGEPEQG PDSHCIPSFCSAPEVPYASLTDIEYLVQNVCKSFRETCQLRLEDLLRQRTNLFSREEVTSYQR KSMWEMWERCAHHLTEAIQYVVEFAKRLSGFMELCQNDQIILLTAGAMEVVLVRMCRAY NANNHTVFFEGKYGGVELFRALGCSELISSIFDFSHFLSALCFSEDEIALYTALVLINANRPGL QEKRRVEHLQYNLELAFHHHLCKTHRQGLLAKLPPKGKLRSLCSQHVEKLQIFQHLHPIVV QAAFPPLYKELFSTDVESPEGLSK (SEQ ID NO:2)

FIGURE 1

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

GGAGGGCAGCAAGGACGGCACCAAGGGAGCTACCCCATGGACAGGGCCCCACAGAGACAC CACCGGACATCTCGGGAGCTGCTGGCTGCAAAGAAGACCCACACCTCACAAATTGAAGTG ATCCCTTGCAAGATCTGTGGGGACAAGTCATCTGGGATCCACTACGGGGTTATCACCTGT GAGGGGTGCAAG [GGCTTCTTCCGCCGCAGCCAGCAGTGTAATGTGGCCTACTCCTGCACG CGTCAGCAGAA] CTGCCCCATTGACCGAACCAGCCGCAACCGATGCCAGCATTGCCGCCTG ${\tt CAGAAGTGCCTGGGCTCTGGGCATGTCCCGAGATGCTGTCAAGTTT}{\tt GGCCGAATGTCCAAGTGTCAAGTGTCCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCCAAGTGTTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGTGTCAAGT$ AAGCAGAGGGACAGTCTACATGCAGAAGTGCAGAAACAACTGCAACAGCAGCAGCAACAG GAACAAGTGGCCAAGACTCCTCCAGCTGGGAGCCGCGGAGCAGACACACTTA [CATACACT TTAGGGCTCTCAGATGGGCAGCTACCACTGGGCGCCTCACCTGACCTACCCGAGGCCTCT GCTTGTCCCCCTGGCCTCCTGAGAGCCTCAGGCTCTGGCCCACCATATTCCAATACCTTG GCCAAAACAGAGGTCCAGGGGGCCTCCTGCCACCTTGAGTATAGTCCAGAACGAGGCAAA GCTGAAGGCAGAGACATCTATAGCACTGACGGCCAACTTACTCTTGGAAGATGTGGA CTTCGTTTTGAGGAAACCAGGCATCCTGAACTTGGGGAACCAGAACAGGGTCCAGACAGC G] AGTACCTGGTACAGAATGTCTGCAAGTCCTTCCGAGAGACATGCCAGCTGCGACTGGAG GACCTTCTACGGCAGCGCACCAACCTCTTTTCACGGGAGGAGGTGACCAGCTACCAGAGG AAGTCAATGTGGGAGATGTGGGAGCGCTGTGCCCACCACCTCACTGAGGCCATTCAGTAT GTGGTGGAGTTTGCCAAGCGGCTTTCAGGCTTCATGGAGCTCTGCCAGAATGACCAGATC ATACTACTGACAGCAGGAGCAATGGAAGTCGTCCTAGTCAGAATGTGCAGGGCCTACAAT GCCAACAACCACAGTCTTTTTGAAGGCAAATACGGTGGTGTGGAGCTGTTTCGAGCC TTGGGCTGCAGCGAGCTCATCAGCTCCATATTTGACTTTTCCCACTTCCTCAGCGCCCTG TGTTTTTCTGAGGATGAGATTGCCCTCTACACGGCCCTGGTTCTCATCAATGCCAACCGT CCTGGGCTCCAAGAGAAGAGGAGAGTGGAACATCTGCAATACAATTTGGAACTGGCTTTC CATCATCTCTGCAAGACTCATCGACAAGGCCTCCTAGCCAAGCTGCCACCCAAAGGA AAACTCCGGAGCCTGTGCAGCCAACATGTGGAAAAGCTGCAGATCTTCCAGCACCTCCAC CCCATCGTGGTCCAAGCCGCCTTCCCNCCACTCTATAAGGAACTCTTCAGCACTGATGTT CCCTCTGACCCGTCTCCCTGGACTCCCTTCACCCAGCCTTTCCCCTTTCTGCACTCTATGA AGGGTGGTATCCCTAGGAGTAAGCAAATCCTAAGACTGATTTTCTGCCCCTAGGCTTGCC TTGTAGGACAACAGCAGCAAGTGATGGAGAAAAGGCTTGTTATGTTTGATTTCCCATAAG TTCCACCCTGGCTTCTGGAAGCTGTGGGGTAGATGGGATAGAGATAGGATGACCAAGTCA AATAAAAAACAGACTGACAATCAGCAGGGATAAATCCAGGTACCTGGGATAAGGAGAACT CAAATCTAGGCTTGAAAGCTAATAACAGTCCTTTCAATACCTCATTGTATTTCCCCATGG GTCCTCCTGGGGGGACATGGATCTAGCTCAGAGACTGGTGGCAAGCCCCCAGAAGGACCT GTATATAATAAGAATATAGATTCCTG (SEQ ID NO:1)

FIGURE 2A

Gene Sequence Structure *

Size of full-length cDNA: 2066 bp

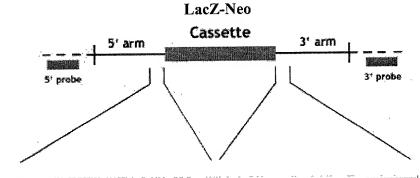
252 bp Sequence Deleted 472 bp

Targeting Vector* (genomic sequence)

Construct Number: 651

Arm Length: 5': 1.6 kb 3': 2.5 kb

Targeting Vector
- - - - Endogenous Locus
* Not drawn to scale



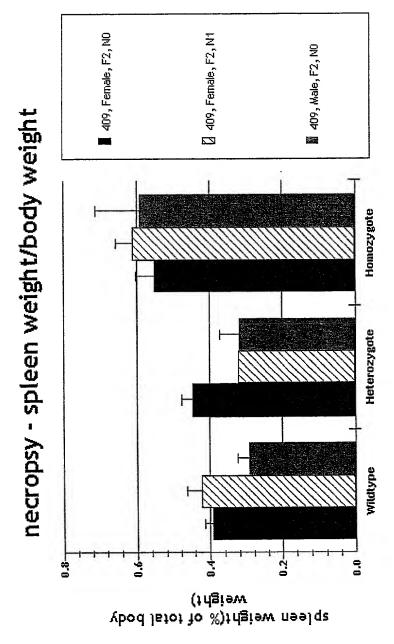
5'>CAGGGTCCATCACAATTATAC
AGTGGAGGTTCGGGGACTTTGGTG
GATGTAGAAATTCTTGAGACCAGT
GCACATGAATTGGAGGTCCCTGGG
ACCACCTCAAACTCCGAGAGGGTG
GGATAAGCAGTTTCTGTTTCCCAG
GGCTTCTTCCGCCGCAGCCAGCAG
TGTAATGTGGCCTACTCCTGCACG
CGTCAGCAGAA<3'

(SEQ ID NO:3)

5'>CATACACTTTAGGGCTCTCAG ATGGGCAGCTACCACTGGGCGCCT CACCTGACCTACCCGAGGCCTCTG CTTGTCCCCCTGGCCTCCTGAGAG CCTCAGGCTCTGGCCCACCATATT CCAATACCTTGGCCAAAACAGAGG TCCAGGGGGCCTCCTGCCACCTTG AGTATAGTCCAGAACGAGGCAAAG CTGAAGGCAGA<3'

(SEQ ID NO:4)

FIGURE 2B



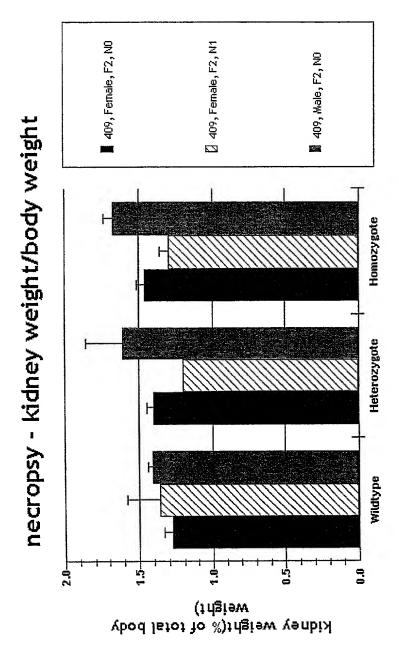
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FIG. 3

Z 409, Female, F2, N1 409, Female, F2, NO 🛮 409, Male, F2, NO necropsy - liver weight/body weight Homozygote Heterozygote liver weight(% of total body weight)

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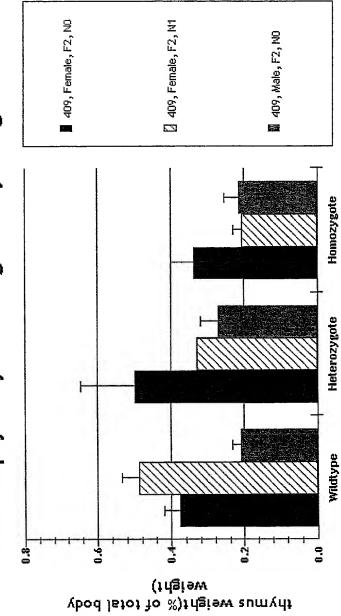
FIG. 4



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FIG. 5

necropsy - thymus weight/body weight



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FIG. 6